EPILEPSY

435 medicine teamwork

[Important | Notes | Extra explanation or example | Editing file]

lecture objectives:

- Definition of epileptic seizure, provoked seizure and epilepsy.
- Status epilepticus.
- Frequent causes of seizure and risk factors.
- Triggers of seizures in epileptic patient.
- Epilepsy classification and seizure semiology.
- DDX of SZ
- Seizure vs syncope
- Approach to seizure disorder (Hx, Ex, inx)
- Medical and surgical management of epilepsy.
- How to select antiepileptic medications.
- When to stop antiepileptic medications.

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References: Davidson's, Slides, Team 434, Master the boards.

SEIZURE and EPILEPSY

Introduction:

Highly recommended video

- **Seizure:** Transient occurrence of signs and symptoms of sudden changes in neurological function due to ABNORMAL EXCESSIVE, synchronous discharge of cortical neurons. (excessive not only abnormal)
- **Provoked seizure:** occurs in the setting of acute medical and neurological illnesses in people with no prior history of seizures. (in this case we have a patient with no history of epilepsy, but he presents with seizure due to e.g CNS infection or an elderly pt with hyponatremia .)
- **Epilepsy:** Recurrent (two or more) unprovoked seizure .
- **Status Epilepticus: (life-threatening).** (any type of seizure can lead to it, the most serious form of SE is GTC).
  - seizure activity not resolving spontaneously
  - prolonged seizure that last for 20-30 min.
  - recurrent seizure with no recovery in between not returning to baseline between 2 seizures (e.g if someone got a seizure 6 AM and he became comatose then he got another seizure at 9 AM and he did not go back to his baseline of consciousness between 6-9 AM, its status epilepticus)
- **seizure is a symptom not a disease like cough it is caused by something else**

TYPES:

you have to understand that the main difference between focal & generalized seizures is that the level of consciousness in generalized seizures is lost. It is very important in treatment & there are other things such as aura that precedes focal seizures.

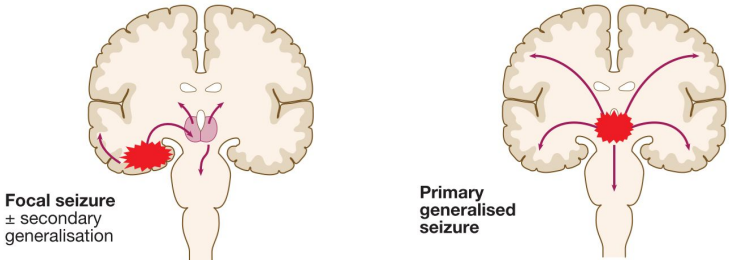
SEIZURES	
Generalized Seizures	**Focal Seizures** (more than 80% in epileptic adults)
Tonic-Clonic seizures (GTC).	Focal 'simple partial' > **without impairment** of awareness or consciousness. E.g. Jacksonian seizure[1]
Absence Seizure. Previously known as "Petit mal epilepsy" it is seen a lot in pediatric & aggravated by hyperventilation	Focal 'Complex partial' > **with impairment** of awareness or consciousness aggravated by sleep deprivation
Myoclonic seizure. seen with juvenile myoclonic epilepsy[2] and aggravated by flashes of light	Focal secondarily generalized > Evolving to a bilateral, convulsive seizure. Tonic, clonic, or tonic-clonic
Atonic seizure.	
Tonic seizure.	
Clonic seizure.	
Unknown seizure	

[1] Jacksonian seizure is a type of simple partial seizure characterized by abnormal movements that begin in one group of muscles and progress to adjacent groups of muscles.

[2] Juvenile myoclonic epilepsy (JME) is an idiopathic generalized epileptic syndrome characterized by myoclonic jerks, generalized tonic-clonic seizures (GTCSs), and sometimes absence seizures

Epileptic spasm mainly associated with infants

How is primary generalized seizures different from secondary generalized seizures?



A focal seizure originates from a paroxysmal discharge in a focal area of the cerebral cortex (often the temporal lobe); the seizure may subsequently spread to the rest of the brain (secondary generalisation) via diencephalic activating pathways. In primary generalised seizures the abnormal electrical discharges originate from the diencephalic activating system and spread simultaneously to all areas of the cortex.

Semiology:

Seizure Semiology "Study of signs"	
Tonic-Clonic seizures **"Grand mal seizures"**	Initial "aura" that depends on which cortical area the seizure originate > Then patient becomes Rigid (Tonic) and unconscious > Then fall (risk of facial injury). Breathing stops and central cyanosis may occur > As cortical discharge reduced in frequency > jerking movement (clonic) is produced > Then, flaccid state of deep coma that persists for minutes.
Absence Seizure img **"Petit mal seizures"**	Characterized by 3 to 30 seconds of unconsciousness (or diminished consciousness) during which time the person has twitch-like contractions of muscles usually in the head region, especially blinking of the eyes; this is followed by return of consciousness and resumption of previous activities.
Myoclonic Seizure img	Brief jerking movements predominate in Arms. (usually single jerky movement)
Atonic seizure img	Loss of muscle tone > results in falling with or without loss of consciousness
Tonic seizure img	Generalized increase in muscle tone associate with loss of awareness
Clonic seizure img	generalized multiple jerking movements

Pathophysiology:

- Attacks occur when the basal level of excitability of the nervous system (or part of it) rises above a certain critical threshold. As long as the degree of excitability is held below this threshold, no attack occur.
- Brain functions normally in balance between Excitation (e.g. Na, amino acids "glutamate" and "aspartate") and Inhibition (Gamma-aminobutyric acid "GABA"). Imbalance between excitation and inhibition will induce seizure. " MOA of antiepileptic drugs work by either reducing the excitability or enhance the inhibition"
- Seizures may be local or generalized.
- Seizures that are at local areas produce symptoms related to area that involved. Any architectural or functional disturbance (e.g. Infection, tumor, scarring) would precipitate this.
- Seizures that are generalized may originate from central mechanisms that control cortical activation and spreads rapidly. This type may reflect widespread disturbance structurally or functionally.
- **What Stops the Generalized seizures "Grand Mal Attack"?**
    1) Neuronal fatigue.
    2) Active inhibition by inhibitory neurons that have been activated by the attack.

Seizure is initiated when excitation rises to a certain threshold > patient seize. why do seizures stop after seconds or minutes? because of neuronal fatigue and stimulation of inhibitory neurons.

Clinical Features:

Clinical Features of Focal Seizures (it is very important, dr said he will give us a scenario & ask which lobe is affected)	
Temporal lobe	Impaired awareness. preceding oral or hand automatism
Frontal lobe	Produce bizarre behavior pattern (sleepwalking, limb posturing) hypermotor seizure during sleep
Occipital lobe	Visual changes
Sensory area	Sensory alteration such as Burning or Tingling sensation
Motor area	Jerky movement
Portion of Limbic system **"Psychomotor seizure".**	Amnesia; abnormal Rage; sudden Anxiety, Discomfort, or Fear; and/or moment of Incoherent Speech or mumbling of some trite phrase.

Causes and Triggers:

SEIZURES		
Risk factors for developing Epilepsy	**Triggers** (in a patient with a diagnosis of Epilepsy يعني هو مريض إبالابيلبسي و هذي بتحفز انه يجيه صرع)	**Causes** "VITAMINS"
❖ Febrile convulsion (main risk factor for Hippocampal Sclerosis) Patients who get febrile between the age of 6 months to 6 years and develop a seizure (febrile convulsions) are at higher risk to have epilepsy later on. But not any child who develops febrile convulsions will have epilepsy, it should be prolonged and recurrent etc. ❖ Perinatal insult The most important cause is infections (TORCH infections e.g toxoplasma and rubella) also it could be because of trauma or drugs. ❖ CNS infection such as meningitis and encephalitis ❖ CNS mass lesion ❖ Family history of epilepsy which means that there is genetic predisposition to epilepsy ❖ Head injury (frontal penetrating trauma is the most & higher in risk) ❖ Abnormal gestation or delivery (prolonged delivery) e.g. cerebral palsy (caused by decreased oxygen supply during delivery) ❖ Developmental delay ❖ Stroke (ischemic or hemorrhagic) any intracranial pathology	❖ Poor compliance may lead to Sudden unexpected death in epilepsy (SUDEP) ❖ Sleep deprivation ❖ Stress ❖ Alcohol ❖ Infection ❖ Menstrual cycle (they will have catamenial seizures)	➔ **V**ascular:(stroke, bleed, arteriovenous malformation) ➔ **I**nfection:(meningitis, abscess, encephalitis) ➔ **T**rauma:(especially frontal, penetrating injuries) ➔ **A**utoimmune:(CNS vasculitis) ➔ **M**etabolic:(hyponatremia, hypocalcemia, hypomagnesemia, hypoglycemia, hypoxia, Hyperthermia, Eclampsia, drug overdose/withdrawal-Alcohol withdrawal, Benzodiazepine withdrawal) ➔ **I**diopathic (65% of all cases) ➔ **N**eoplasm ➔ p**S**ychiatric

Differential Diagnosis of seizure :

- ❖ Transient Ischemic Attacks
- ❖ Syncope
- ❖ Migraine
- ❖ Movement disorders (ex: Tics)
- ❖ Panic attack
- ❖ Psychogenic seizure (last cause to think of)

***you can conclude from seizure definition that the it is transient. So when you think of the differential, think about causes with transient effect.**

Seizure vs Syncope:

Comparison of clinical features in cardiogenic syncope versus seizure disorders

Clinical features	Cardiogenic syncope	Seizure disorders
Loss of consciousness	Typical	Common
Episode duration	Seconds	Minutes
Involuntary movements	Common	Typical
Amnesia	Yes	Yes
Arrhythmia	Common	Rare*
Electroencephalogram	Slow waves Flattening	Focal or general spike activity
Responsive to AEDs	No	Often
Short term mortality†	High	Low

In addition, in cardiogenic syncope the patient's face is pale. While in seizure, the face is cyanosed

Approach for Taking History:

Thanks to 434 Team

What happened:

Q: Was there any warning noted before the spell?

➔ **Before:** aura vs presyncopal prodrome

Q:What did the patient do during the spell?

Q:Was the patient able to relate to the environment during the spell?

➔ **During:** convulsion, automatisms vs brief syncopal blackout and pallor

Q: How did the patient feel after the spell? How long did it take for the patient to get back to baseline condition?

➔ **After:** post-ictal confusion and headache vs rapid recovery in syncope

Q:How long did it last?

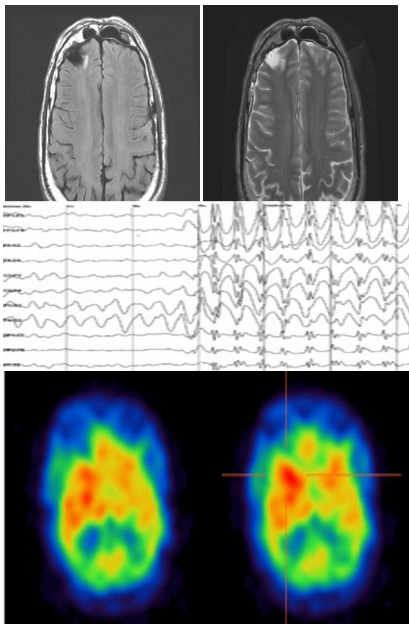
- ***Circumstances***
  - ➔ Seizure triggers? Sleep deprivation, alcohol binge or drugs
  - ➔ Syncope triggers? Pain, heat, prolonged standing, etc.
  - ➔ *Epilepsy risk factors?*
  - Childhood febrile convulsions
  - Significant head injury
  - Meningitis or encephalitis
  - Family history of epilepsy

- ***Previous unrecognized seizures? How frequent do the spells occur?***
  - Myoclonic jerks
  - Absences
  - Auras (simple partial seizures)
- **Alcohol excess?**
- ***Medication lowering seizure threshold?***

after that is examination then investigation

Investigations:

❖ Single seizure



- ◇ 1st: Transient loss of consciousness > ECG
- ◇ 2nd: Suspected seizure? do > CT or MRI:
  - ■ In MRI Look for:
    - ● Tumor, Vascular, Trauma, Developmental, and Mesial Temporal sclerosis.
  - ■ Normal MRI in 80% of seizure (non-lesional)
- ◇ 3rd: Electroencephalogram (EEG) for prognosis.
  - ■ Note from master the boards: There is no point in doing an EEG for a seizure from a brain tumor.
- ◇ Nuclear Medicine
- ◇ Cognitive Testing:
  - ■ Intelligence, Memory (verbal and visual), and language.
- ◇ 4th: other investigation for toxic, infective and metabolic causes.

❖ Epilepsy (known case)

- ◇ EEG and Video EEG monitoring (VEM)
  - ■ helps to establish the type of epilepsy and guides therapy.
  - ■ Inter-ictal EEG is abnormal in 50% of patients, we increase the sensitivity up to 85% by prolonging the recording time. This occurs by Sleep recording or 24h ambulatory EEG.
  - ■ Ambulatory EEG or video EEG help in differentiation between epilepsy and other attack disorders.
- ◇ Imaging (CT or MRI) for detecting focal changes.
- ◇ Lumbar puncture and blood culture > if the patient is febrile
- ◇ Rule out other causes. table (26.40) (don't forget to rule out VITAMINS when a patient with epilepsy came with worsening sx)

26.40 Investigation of epilepsy

From where is the epilepsy arising?

- Standard EEG
- Sleep EEG
- EEG with special electrodes (foramen ovale, subdural)

What is the cause of the epilepsy?

Structural lesion?

- CT
- MRI

Metabolic disorder?

- Urea and electrolytes
- Liver function tests
- Blood glucose
- Serum calcium, magnesium

Inflammatory or infective disorder?

- Full blood count, erythrocyte sedimentation rate, C-reactive protein
- Chest X-ray
- Serology for syphilis, HIV, collagen disease
- CSF examination

Are the attacks truly epileptic?

- Ambulatory EEG
- Videotelemetry

26.41 Indications for brain imaging in epilepsy

- Epilepsy starting after the age of 16 yrs
- Seizures having focal features clinically
- EEG showing a focal seizure source
- Control of seizures difficult or deteriorating

Management:

Immediate care

- Move the person away from any danger.
- After convulsions cease, Turn person into 'recovery' position (semi-prone). img
- Do not insert anything in the mouth and make sure the airway is clear.
- If convulsions continue for more than 5 mins seek urgent medical attention.
- Do not leave the person alone until fully recovered.

Medical Management

26.46 Guidelines for choice of anti-epileptic drug

Epilepsy type	First-line	Second-line	Third-line
Focal onset and/or secondary GTCS	Lamotrigine	Carbamazepine Levetiracetam Sodium valproate Topiramate Zonisamide Lacosamide	Clobazam Gabapentin Oxcarbazepine Phenobarbital Phenytoin Pregabalin Primidone Tiagabine
GTCS	Sodium valproate Levetiracetam	Lamotrigine Topiramate Zonisamide	Carbamazepine Phenytoin Primidone Phenobarbital Acetazolamide
Absence	Ethosuximide	Sodium valproate	Lamotrigine Clonazepam
Myoclonic	Sodium valproate	Levetiracetam Clonazepam	Lamotrigine Phenobarbital

N.B. Use as few drugs as possible at the lowest possible dose.

1st line is the most imp to know

¨1st drug ---------- seizure free (47%)
¨2nd drug---------- seizure free (14%)
¨3rd drug---------- seizure free (3%) We often use only two drugs because, as you can see, addition of a 3rd drug shows improvement in only 3% of the cases. In addition, when we add a drug we put the patient at higher risk of developing ADRs and the MOA of the three drugs will interfere with each other.

Use of single drug is preferred when possible, because of risk of pharmacokinetic interactions.
Anti-epileptic drugs (AEDs) should be used after more than one unprovoked seizure. Their MOA is either increasing the negativity[3] of neurotransmission or decreasing the positivity (excitement) neurons by blocking sodium channels. (70% of epileptic pts are well controlled by drugs while 30% are refractory "more than 2 attacks by 6 months" which we refer to surgery)

Lamotrigine is the drug-of-choice with minimal side effects, but shouldn't be used with oral contraceptives because it reduces its efficacy **(MCQ: what is the drug of choice in case of absence seizures ? ethosuximide or valproic acid .**

MCQ: phenytoin and carbamazepine aggravates absence and juvenile myoclonic epilepsy)

Sodium Valproate is BEST for unclassified or specific syndromes. Not used in pregnancy.

Measuring serum levels of drugs is only indicated when there's doubt whether the patient is taking the medications or not. Because the new drugs have more predictable pharmacokinetic than the older.

[3] increasing the negativity is achieved by:
Enhancing GABA. This may be achieved by
inhibiting GABA-transaminase
Or by drugs with direct GABA-agonist properties.

Drug resistant epilepsy: Failure of at least TWO antiepileptic medications to completely control seizures.

Other Management

- Vagal Nerve Stimulation
- Deep Brain Stimulation
- Patients who experience seizure despite taking medication, should undergo surgical resection of epileptogenic area of the brain. But planning to such intervention should undergo an intensive specialist assessment. Hemispherectomy in Rasmussen's encephalitis

Epilepsy and WOMEN

Anti-epileptic drugs induce hepatic enzymes that metabolize contraception synthetic hormones, this increase the risk of contraception failure. This occurs with Phenytoin, Barbiturates, carbamazepine, and significant with lamotrigine and topiramate. Sodium Valproate has no interaction.

Anti-epileptic drugs (AEDs), especially Sodium Valproate, is teratogenic[4], and causes menstrual irregularities, reduce fertility and osteoporosis. During pregnancy, using Folic acid and decreasing the dose of AEDs may reduce the incidence of teratogenesis.

Lamotrigine has the lowest incidence of fetal malformations. (safe in comparison with other AEDs)

Lifestyle Modification

- Avoid activities where they might place themselves or others at risk if they have a seizure. These include activities requiring prolonged proximity to water, prolonged cycle journeys.
- Certain occupations, such as firefighter or airline pilot, are not open to anyone who has an active diagnosis of epilepsy.
- Driving precautions.

Withdrawing Anti-Epileptic Drugs

Withdraw anti-epileptic drugs can be done after 2 seizure-free years (dr said 3 years while davidson 2)
Withdraw should be slowly and over months. Childhood-onset seizures carry best prognosis and the adult-onset have tendency to recur. Patient should know the complication to decide.

Status Epilepticus "MEDICAL EMERGENCY"

[4] -The risk of teratogenicity is well known (~5%), especially with valproates, but withdrawing drug therapy in pregnancy is more risky than continuation.
-Over 90% of pregnant women with epilepsy will deliver a normal child.

- ABC
- Evaluate and treat any precipitating causes of seizure
- If the patient continues to seize, the initial drug of choice is Benzodiazepines (lorazepam or diazepam).
- continues to seize? > add phenytoin or Fosphenytoin.
- continues to seize? > add phenobarbital.
- continues to seize? > add midazolam or propofol.
- The longer the duration, the greater the risk of permanent cerebral damage.

MCQs

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1) which of the following is the drug of choice in case of absent seizure?

a. Ethosuximide
b. Sodium Valproate
c. Lamotrigine
d. Phenytoin

2) A 71-year-old man with atrial fibrillation is seen in clinic following an episode of syncope. He describes getting a poor night's sleep and, as he got out of bed in the morning, feeling dizzy for a couple of seconds before the lights dimmed around him. He was woken a couple of seconds later by his wife who had witnessed the event. She says he went pale and fell to the floor and his arms and legs jerked. After waking, he was shaken but was 'back to normal' a few minutes after the event. His medication includes aspirin, atenolol and furosemide. What is the most likely diagnosis?

a. Vasovagal syncope
b. Orthostatic hypotension
c. Cardiogenic syncope
d. Transient ischaemic attack (TIA)
e. Seizure

3) A 17-year-old girl is brought into accident and emergency with generalized tonic-clonic seizure. Her mother had found her fitting in her bedroom about 20 minutes ago. The ambulance crew handover state that her sats are 96 per cent on 15 L of oxygen and they have given her two doses of rectal diazepam, but she has not stopped fitting. What is the most appropriate management?

a. Lorazepam.
b. Phenobarbital
c. Intubation
d. Call ITU
e. Phenytoin loading

4) A 23-year-old woman is seen in clinic for recurrent funny turns. She is not aware of them, but her family and friends have noticed them. They say she looks around blankly, then starts picking at her clothes and sometimes yawns, then she comes back after a minute. She can get drowsy after these episodes. What seizure type does this patient describe?

a. Absence.
b. Tonic clonic
c. Simple partial
d. Complex partial
e. Generalized

Answer key:
1 (A) | 2 (B) | 3 (E) | 4 (D) |

MCQs Answers explanation

2)**B.** This man most likely experienced an episode of orthostatic or postural hypotension (**B**) where syncope occurs as a result of reduced cerebral perfusion as the patient moves from lying to standing. Symptoms are similar to vasovagal in that the patient may become pale and describe 'the lights or sound dimming'. Perfusion is restored after the patient collapses and unconsciousness lasts no more than seconds or a couple of minutes with full recovery. However, vasovagal episodes (**A**) can be brought on by sleep or food deprivation, hot or emotional environments, Valsalva manoeuvre (such as straining) and are not as closely related to position. Syncope while lying down is more suggestive of cardiac syncope or seizure activity. It is important to rule out cardiac causes of syncope (**C**) which may be heralded by chest pain or palpitations. Arrhythmias or aortic stenosis may be the underlying cause. TIAs (**D**) are a very rare cause of syncope. Seizures (**E**) may be triggered by lack of sleep. They may be heralded by an aura, typically visual or olfactory. There may be urinary incontinence, tonic-clonic movements, tongue-biting and cyanosis during the event. However, jerky movements may occur in syncope of any cause. This alone does not equate to a seizure.

3)**E.** Status epilepticus is a serious condition of continuous seizure activity lasting more than 30 minutes. The mortality rate is one in five. This girl has been fitting for at least 20 minutes despite two doses of diazepam so must urgently be loaded with phenytoin (**E**) and monitored closely. ITU (**D**) should be alerted in case phenytoin does not stop the seizure in which case phenobarbital (**B**) can be considered, but the phenytoin should be given first. Ultimately, general anaesthetic and intubation (**C**) may be required. There is increasing evidence that lorazepam (**A**) is more effective than diazepam, but in this case the patient has already had two doses of benzodiazepine so the next step is phenytoin infusion.

4)**D.** This woman has complex partial seizures (**D**) which start focally in the brain (classically temporal lobe) and by definition result in reduced awareness. Patients do not remember the seizure, unlike simple partial seizures (**C**) where consciousness is maintained. Automatisms typically characterize complex partial seizures where patients carry out repetitive and seemingly purposeless actions such as chewing, lip-smacking, picking and fumbling. Absence and tonic-clonic are types of generalized seizures (**E**). Absence seizures (**A**) typically occur in children and last seconds. Children are reported as 'staring blankly'. Seizures can be difficult to detect as they can be subtle, short-lived and the child is unaware of them. Tonic-clonic (previously called grand mal) (**B**) are the classic seizures where patients fall to the ground unconscious and then go through a tonic (tensing) then clonic (jerking) phase lasting seconds to minutes, typically associated with tongue-biting and incontinence and post-ictal drowsiness. Complex partial seizures may subsequently generalize but this has not been reported by this patient. Carbamazepine, lamotrigine and valproate are first-line monotherapy.

Just for your knowledge you do not need to know it, this is the latest classification of seizure types